

Doppler assessment of fetal well-being – A rational approach

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ABSTRACT

Doppler sonography provides insight into the uteroplacental and fetoplacental circulation non-invasively. It has important diagnostic implications in fetal growth restriction (FGR), monitoring of multiple pregnancies complicated by discordancy and placental vascular communications in twin-to-twin transfusion syndrome (TTTS), and fetal anemia; particularly, red blood cell isoimmunization in Rh-negative pregnancies. There is a sequence of changes in UA Doppler velocimetry whenever there is fetal compromise, that is, increased S/D ratio, centralization of flow (brain-sparing effect) followed by absent end-diastolic flow and finally reversed end-diastolic flow. When venous Doppler studies {e.g., umbilical vein (UV), ductus venosus (DV), and inferior vena cava (IVC) Doppler} also become abnormal, perinatal mortality and still birth increase manifold. Vertebroplacental ratio (VPR) is proved to be an alternative to cerebroplacental ratio (CPR) in fetal surveillance near term. DV flow assessment in the first trimester has a vital role in screening for chromosomal abnormalities and cardiac defects.

Key words: Doppler USG, End-diastolic flow, Fetal anemia, Fetal growth restriction, Umbilical artery

Doppler sonography has become a part of routine antenatal surveillance in obstetrics in the past 3 decades since the pioneering work of FitzGerald, *et al.* [1] which introduced Doppler ultrasonography in obstetrics. Doppler sonography provides insight into the uteroplacental and fetal arteriovenous circulation non-invasively. In principle, Doppler interrogation says that echoes returning from moving structures are altered in frequency and amount of shift is directly proportional to the velocity of moving structure. The vessels usually subjected to this are uterine artery, umbilical artery (UA), middle and anterior cerebral artery, aortic isthmus, umbilical vein (UV), ductus venosus (DV), and inferior vena cava (IVC) [2].

When vascular resistance is normal, sizeable blood flow occurs during diastole, but in case of increased resistance, diastolic flow decreases to minimal. Doppler study of selected fetal organ is valuable in detecting the hemodynamic rearrangements that occur in response to fetal hypoxemia, whereas investigation of the uterine and umbilical arteries gives information on the perfusion of the uteroplacental and fetoplacental circulations, respectively. Doppler assessment has established its foothold firmly in many areas of perinatology and it has important diagnostic implications in fetal growth restriction (FGR), monitoring of multiple pregnancies complicated by discordancy, growth restriction, and

placental vascular communications in twin-to-twin transfusion syndrome (TTTS), fetal anemia; particularly, red blood cell isoimmunization in Rh-negative pregnancies complicated by hydrops and IUT (*In utero* transfusion) and likely role in maternal diabetes mellitus (Pre-gestational diabetes: >Class C or vasculopathy), maternal autoimmune vascular diseases (SLE and APL), post-term pregnancy, and diagnosis of fetal anomalies (i.e., screening for aneuploidies and cardiac defects, status of renal vessels in renal malformations, intracranial arteriovenous fistulae [such as vein of Galen malformation and in distinguishing this vascular anomaly from an arachnoid cyst, porencephaly, or hydrocephaly], thoracic space occupying lesions like bronchopulmonary sequestration).

MATERIALS AND METHODS

We searched PubMed, Cochrane Central Register of Controlled Trials, Google Scholar, MEDLINE, and EMBASE up to November 2020; and previous literature reviews including cross references and abstracts. Combining the terms Doppler [All Fields] AND (“Assessment” [Journal] OR “assessment” [All Fields]) AND (“fetus” [MeSH Terms] OR “fetus” [All Fields] OR “fetal” [All Fields]) AND well-being [All Fields] yielded 491 results. We included individual case reports with literature reviews, case series, and systemic reviews. The results of retrieved articles

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were reviewed for potentially relevant studies, and we selected articles dealing with Doppler ultrasonography of maternal and fetal blood vessels in fetal surveillance and its prospective usage in fetal management.

MATERNAL AND FETAL VESSELS ON WHICH DOPPLER STUDY IS DONE FOR FETAL SURVEILLANCE

Uterine Artery Doppler

It is an index of quality of the uteroplacental circulation. With increased resistance, increased S/D ratio, and/or early diastolic notch appear in waveforms. The unilateral uterine artery notch is associated with increased perinatal morbidity, while the bilateral uterine artery notch shows high fetal risk in pregnancies complicated by preeclampsia or fetal growth retardation.

UA Doppler

It reveals the presence or absence of placental resistance to blood flow from the fetus to the placenta [3]. During normal pregnancy, UA is a low resistance vessel and with abundant diastolic flow. Poorly functioning placentas with extensive vasospasm or infarction have an increased resistance to flow in fetal diastole. Prerequisites of obtaining good waveforms are fair selection of the site of probing to obtain waveform and sleeping fetus while taking the measurement. The adequate site is the middle of cord floating in the amniotic fluid (AF). At least 3–4 waveforms should be averaged to obtain a result.

MCA Doppler

Under normal conditions, middle cerebral artery (MCA) is a high impedance vessel and shows minimal diastolic flow. MCA Doppler is an accurate noninvasive test for the diagnosis of fetal anemia and FGR [4]. The USG probe is used to obtain a view adequate for the measurement of biparietal diameter. First vascular structures are identified with color Doppler and then MCA is interrogated a few mm at its origin from the internal carotid artery.

Fetal Aortic Isthmus

Aortic isthmus blood flow measurement by Doppler is a promising tool that helps in early identification of fetal circulatory compromise and assessment of cardiac function in fetuses at risk of developing cardiac failure. Rizzo *et al.* [5] showed that changes in aortic isthmus Doppler velocity waveforms appear before the DV “a” wave reversal and abnormal PI in aortic isthmus is noted around 1 week earlier than the DV.

DV and IVC

Assessment of DV and IVC waveforms gives information about the venous side of fetal circulation. Doppler waveform from DV shows

continuous forward flow with two distinct peaks corresponding to systolic and diastolic phases of cardiac cycle and a nadir corresponding to atrial contraction. During ventricular systole, there is rapid forward flow from DV to RA as atria relaxes [6]. With atrial contraction and active stage of ventricular filling, the foramen closes and resistance to flow are shown by a nadir in DV waveform. Normally, it shows continuous uninterrupted flow during systolic and diastolic phase of the cardiac cycle. Abnormal waveforms in DV are characterized by interruption of forward flow and reversal of flow in the atrial phase of cardiac contraction. Fetal DV flow assessment can be helpful in first-trimester screening for aneuploidic anomalies and second-trimester scanning when there are issues related to FGR and fetal cardiac compromise [7]. Hecher *et al.* [8] studied blood flow in the DV, IVC, and right hepatic vein in 143 normal fetuses and established reference ranges in indices for venous waveform analysis.

UV Doppler

Pulsations in the UV were defined as rhythmic reductions in blood velocity of more than 15% of the baseline velocity [9]. They are present in early weeks of pregnancy and normally disappear by the end of first trimester probably due to changes in cardiac filling patterns. Pulsations are seen in severely growth retarded fetus. Pulsations in the second and third trimesters are a characteristic sign of fetal heart failure and imminent asphyxia and have a high fetal morbidity and mortality. Double pulsation is known to be a more severe sign of fetal compromise and a direct reflection of pulsations in the central veins due to opening of the DV, either due to hypoxia or increased central venous pressure [10].

There are several different ratios for the measurement of flow impedance independent of the angle of insonation, namely, S/D ratio, PI, and RI.

- (i) S/D ratio: It is ratio of systolic to diastolic velocity. UA S/D ratio decreases as pregnancy advances and reaches its lowest value after 36 weeks of gestation. It is <4 before 30 weeks gestation and <3 after 30 weeks gestation in UA [11].
- (ii) PI (pulsatility index): It is systolic-diastolic/mean velocity. The advantage of PI is that even in the absence of diastolic flow or reversal of diastolic flow, numerical value can be obtained. In European countries, PI is used more frequently instead of S/D ratio. Normal value in UA is 1–1.5 [11].
- (iii) RI (Resistance index, also called resistive index or Pourcelot's index) – It is measured as systolic velocity – diastolic velocity/ systolic velocity. Normal value in UA is < 0.8 [11].
- (iv) UA PI and RI show a gradual fall with the gestational age with a strong negative correlation. The fetal MCA PI and RI show a parabolic curve with plateau at 28–30 weeks of gestation. CP ratio also shows a parabolic curve with change between 31 and 32 weeks of gestation [7,11].

Clinical Applications

- (i) **Fetal Growth Restriction:** Conventional fetal biometry is more sensitive in identifying FGR as fetal size is better

assessed by USG measurement of fetal dimensions than by Doppler velocimetry which can assess the hemodynamic condition. Doppler velocimetry of UA and MCA shows fetal hemodynamic alterations much before FHR and BPP monitoring [12]. It follows a characteristic sequence of Doppler changes. The first sign is increase in UA S/D ratio indicating increased UA resistance. By this time, MCA S/D ratio is normal, which is higher than UA S/D ratio. It is followed by the centralization of flow or brain sparing effect which is characterized by increased blood flow to fetal brain and decreasing MCA S/D ratio. MCA S/D ratio becomes lower than UA S/D ratio. On an average, the time interval between the onset of abnormal umbilical arterial Doppler results and the onset of late fetal heart rate decelerations is roughly 2 weeks, but this interval varies considerably among fetuses. Moreover, this interval gets shorter in later than early pregnancy and with hypertensive disease [12,13].

The sequence of events as picked up by UA Doppler in the course of progressive placental lesion and increased fetal demands/fetal compromise is as follows:

- Increased UA resistance denoted by increased S/D ratio without centralization of flow indicated by normal S/D ratio in MCA.
- Increased UA resistance denoted by increased S/D ratio with centralization of flow (brain sparing effect) indicated by decreased S/D ratio in MCA.
- Absent umbilical artery diastolic flow – Further, deterioration leads to a stage where UA blood flow occurs only during systole (Fig. 1). Oxygen supply to fetus is further decreased and metabolic acidosis supervenes. Cardeux *et al.* [14] in their systemic review found markedly increased risk for fetal death in <34 weeks growth-restricted fetuses, particularly those with either umbilical artery or DV absent or reversed end-diastolic velocities.
- Reversed umbilical artery diastolic flow – Indicates extremes of vascular resistance where blood flow is reversed during diastole (Fig. 2). It is an ominous sign necessitating prompt delivery and associated with a high perinatal mortality [15].
- Alterations in the venous side of fetal circulation.

An additional method is the ultrasonographic assessment of the cerebroplacental ratio (CPR). Low CPR near term has emerged as a marker of fetal adverse outcome [16]. The need for operative delivery for fetal compromise, intrapartum fetal distress, admission to the NICU, stillbirths, perinatal deaths, and neonatal morbidity is significantly associated with a low cerebroplacental ratio [17]. Recently, Morales, *et al.* have studied vertebral artery Doppler and demonstrated vertebra-placental ratio (VPR) as an alternative to CPR in fetal surveillance near term. Furthermore, in the evaluation of fetal well-being, VPR behaves as a valid alternative to CPR [18].

In progression from compensation to decompensation, fetal venous circulation starts compromising as hypoxic condition continues. There is a strong correlation between fetal acidemia and poor neonatal outcome, if there is interrupted forward flow

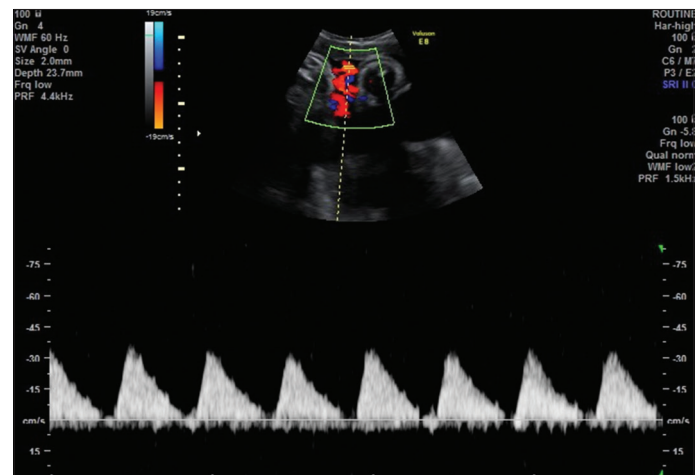


Figure 1: Absent diastolic flow in UA

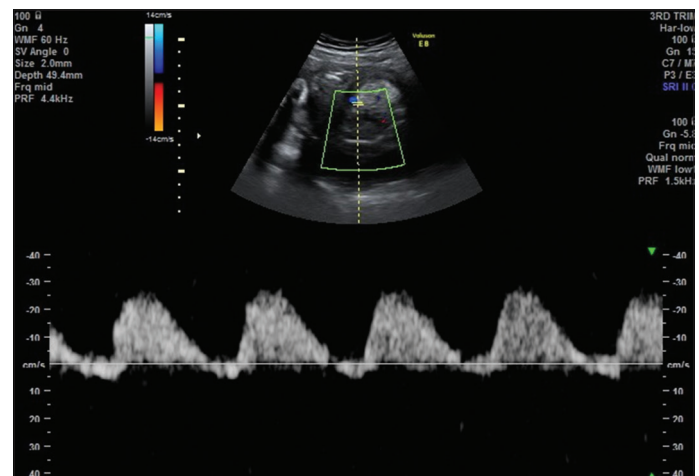


Figure 2: Reversed diastolic flow in UA

in DV, increase in reverse velocity during atrial contraction in IVC, and presence of end-diastolic pulsation in UV [19]. Venous Doppler is useful when used together with FHR monitoring and UA Doppler in fetal surveillance of FGR cases. In growth-restricted fetuses with increased placental blood flow resistance shows elevated index, absent “a” wave and then reversed “a” wave as fetal circulatory compromise progresses [6,14,15,19] (Fig. 3).

In UV – elevation of central venous pressure and worsening status is reflected by progressive pulsatility – monophasic, diphasic, and triphasic pulsatility [9,10].

- Fetal Anemia:** Measurement of fetal hemolysis in Rh alloimmunized pregnancies using spectrophotometry of AF is replaced by widespread use of MCA-PSV. The threshold for the diagnosis of fetal anemia is equal to or greater than 1.5 multiples of median (MoM) for the gestational age (Fig. 4). Chasing MCA-PSV avoids unnecessary cordocentesis [20]. American College of Obstetricians and Gynecologists [21] has recommended measuring MCA-PSV longitudinally in the diagnosis of fetal anemia.
- Multiple Gestations with Growth Restriction and TTTS:** In twin pregnancies, abnormal DV flow is associated with chromosomal abnormalities and cardiac

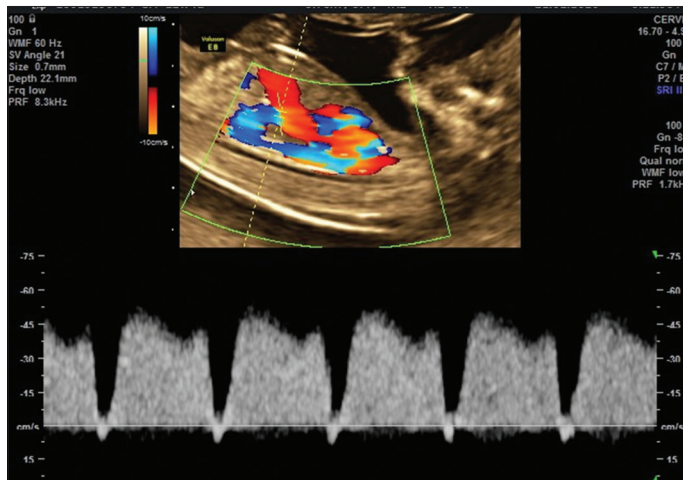


Figure 3: Reversal of “a” wave in DV

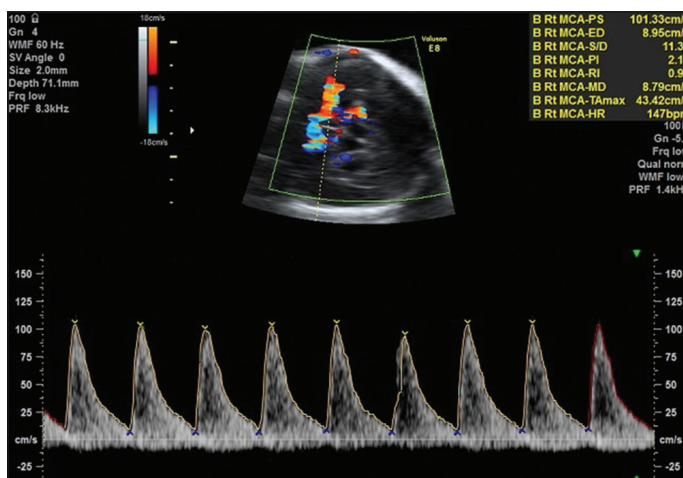


Figure 4: MCA-PSV >1.5 MoM indicating fetal anemia

defects. In monozygotic twins, abnormal flow in the DV in at least 1 of the fetuses increases the risk of developing TTTS [8]. Increased impedance to flow in the umbilical arteries in multiple gestations is a useful predictor of the subsequent development of FGR and adverse perinatal outcome. Qunitero, *et al.* [22] proposed a staging system for TTTS and its role in assessing the severity. This staging involves Doppler USG of UA, UV, and DV along with other USG findings and helps in individualizing the various treatment options, that is, laser ablation procedure.

(iv) **Fetal Anomalies:** DV flow assessment in the first trimester has an important role in screening for chromosomal abnormalities and cardiac defects both in singleton and in twin pregnancies. In chromosomally normal fetuses with increased fetal NT (nuchal translucency), the finding of absent or reversed a-wave in the DV is associated with a 3-fold increase in the likelihood of major cardiac defect [8]. Doppler ultrasonography has been proved very useful in the interpretation of the status of renal vessels in renal malformations, intracranial arteriovenous fistulae, (such as vein of Galen aneurysm and in distinguishing this

vascular malformation from an arachnoid cyst, porencephaly, or hydrocephaly), and thoracic space occupying lesions like bronchopulmonary sequestration.

Doppler-Guided Management in FGR and Fetal Anemia

a. Management in FGR: Management goals in IUGR are prevention of still birth and timely decision to deliver the fetus based on an accurate assessment of fetal versus neonatal risks. Once the diagnosis of FGR is confirmed by fetal biometry while monitoring fetal growth serially, fetal surveillance should be started in form of weekly UA Doppler with or without NST and BPP. If the UA S/D ratio is increasing, more intensive fetal surveillance is warranted with weekly umbilical Doppler USG and twice weekly NST and BPP. Findings of (i) reversal of end-diastolic velocity, (ii) absent or reversed “a” wave in DV, and (iii) pulsatile flow pattern in UV mandates daily Doppler USG testing. When fetal surveillance tests indicate fetal compromise (non-reactive NST, poor fetal HR baseline variability, persistent late decelerations, oligohydramnios, or BPP score <4), delivery should be strongly considered (Fig. 5). Furthermore, in the presence of reversed end-diastolic velocity or other ominous fetal monitoring signs, cesarean delivery is the intervention of choice as fetal tolerance to labor is expected to be poor.

In AEDF:

- (i) If the pregnancy is >34 weeks – consider for delivery.
- (ii) If pregnancy is between 28 and 34 weeks.
 - (a) Conservative approach with weekly or twice weekly UA Doppler, NST, and BPP.
 - (b) ANS to mother.
 - (c) When 1 or more tests indicate imminent fetal danger – deliver the baby.

In REDF: (i) If the gestation is >28 weeks – daily testing of UA Doppler with NST/BPP and immediate delivery in case of imminent fetal compromise.

In both AEDF and REDF – If the gestational age is < 28 completed weeks and with extreme prematurity, the optimal timings for delivery remain uncertain. This needs a pragmatic approach with individualized plan of care considering all relevant clinical factors and counseling of mother and family. Two multicentric prospective randomized control studies worth mentioning at this juncture are Growth Restriction Intervention trial [23] and Trial of Randomized Umbilical and Fetal Flow in Europe trial [24]. Both these multicenter studies failed to reach any concrete conclusion of immediate versus deferred delivery of preterm babies with suspected fetal compromise. Stock, *et al.* [25] cited insufficient evidence on benefits or harms of either of the two interventions, immediate (with or without waiting for 24–48 h for administration of antenatal steroids) delivery versus expectant management and delayed delivery in their Cochrane Database Systematic Review on “Immediate versus deferred delivery of the preterm baby

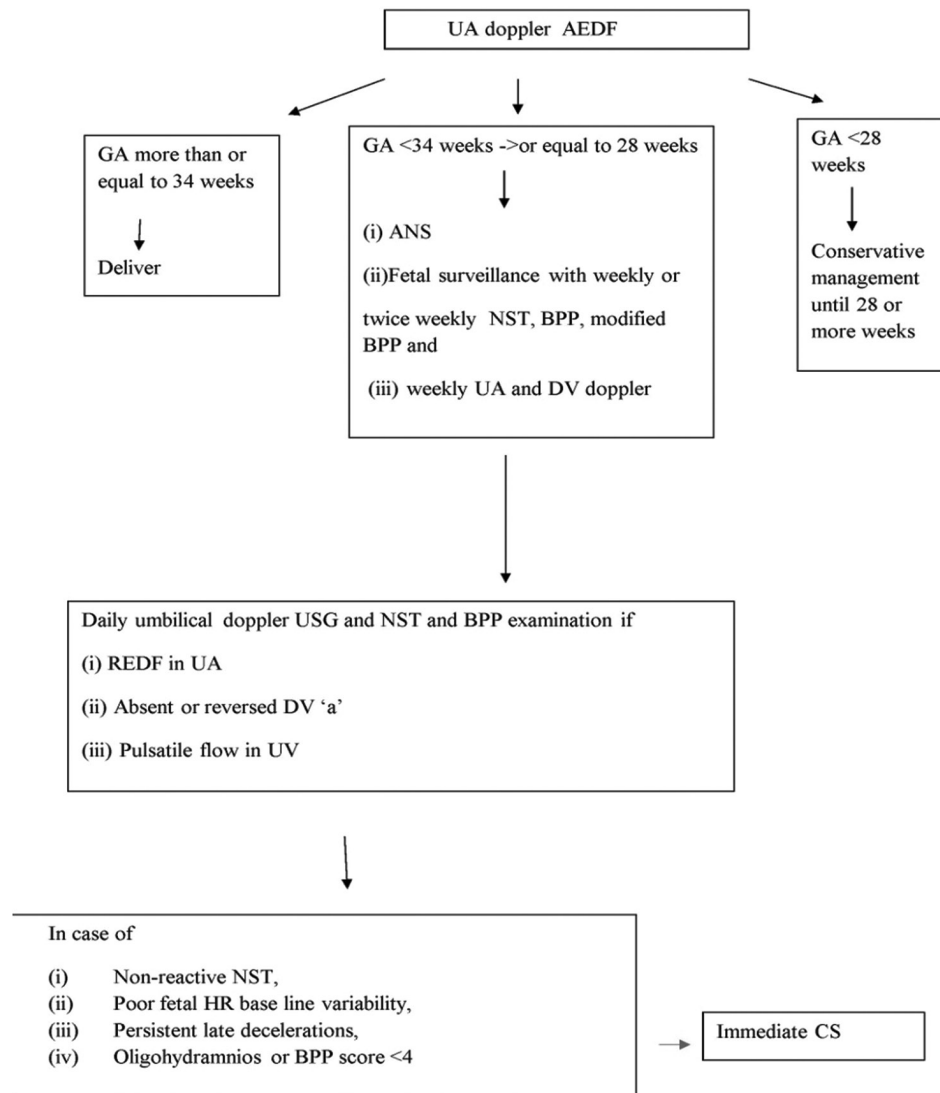


Figure 5: Algorithm for management in fetal UA AEDF

with suspected fetal compromise for improving outcomes.” However, authors noted a trend toward decreased still birth rate with immediate delivery albeit with a possible increase in the neonatal mortality.

b. Management in Fetal Anemia: MCA-PSV > 1.5 MoM detects all cases of significant anemia and avoids unnecessary cordocentesis. Fig. 6 depicts an algorithm in the management of fetal anemia. In a prospective multicenter study of 165 fetuses with red cell alloimmunized pregnancies, Oepkes, *et al.* noted MCA-PSV as an investigation modality, diagnosed anemia in 65 out of 74 cases, whereas previous standard method of delta OD450 did it in only 56 out of 74 cases of anemic fetuses. Results of both the methods were compared with invasive cordocentesis [26].

Alfirevic, *et al.* in their Cochrane Database Systematic Review on “Fetal and Doppler ultrasound in high-risk pregnancies” [27] suggested the use of Doppler ultrasound in high-risk pregnancies for its role in reducing the risk of perinatal deaths and leading to less obstetric interventions.

Key Messages

1. Doppler USG has become a routine in fetal surveillance.
2. It has cardinal role in management of FGR, fetal anemia, multiple gestations (discordancy, TTTS, and FGR), and fetal anomalies.
3. Diastolic notch in uterine artery is associated with pregnancy-induced hypertension, fetal growth retardation, and perinatal mortality.
4. There is a sequence of changes in UA Doppler velocimetry, that is, increased S/D ratio, centralization of flow (brain-sparing effect) followed by AEDF and finally REDF.
5. REDF in UA is a grave sign of fetal jeopardy and associated with a high perinatal mortality.
6. When venous Doppler studies (e.g., DV, UV, and IVC Doppler) become abnormal, perinatal mortality and still birth increase manifold.
7. MCA-PSV > 1.5 MoM is strongly associated with fetal anemia.
8. DV flow assessment in the first trimester has a vital role in screening for chromosomal abnormalities and cardiac defects.

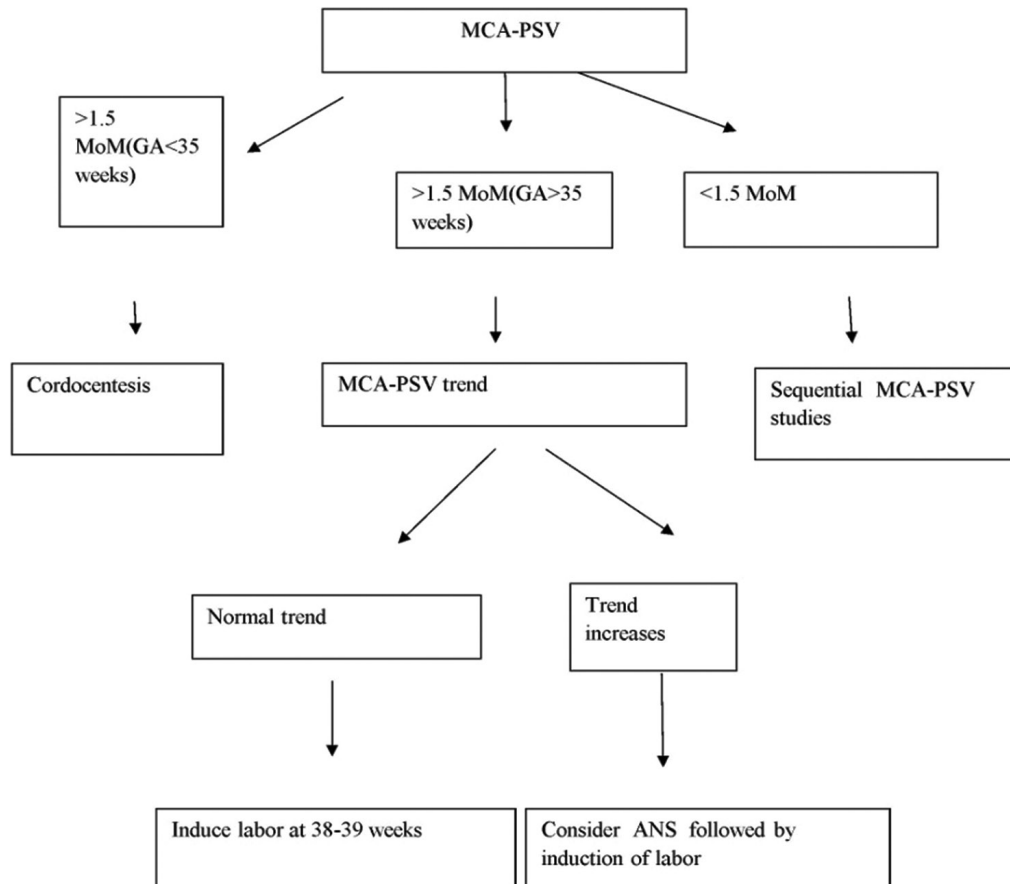


Figure 6: Algorithm for diagnosis of fetal anemia and red cell alloimmunization based on MCA-PSV

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